

Applicants: Jane H. Morse and James A. Knowles  
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**Amendments to the claims:**

Certain claims have been amended and others canceled below without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a continuation application.

The following listing of claims will replace all prior versions, and listings, of claims in the application.

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Listing of claims:

1-3. (canceled)

4. (amended) The method of claim ~~1~~64, wherein the pulmonary hypertension is Primary Pulmonary Hypertension.

5. (original) The method of claim 4, wherein the Primary Pulmonary Hypertension is Familial Primary Pulmonary Hypertension.

6-55. (canceled)

56. (allowed) A method of detecting whether a subject is either predisposed to, or afflicted with, Familial Primary Pulmonary Hypertension which comprises:

- a) obtaining a suitable nucleic acid sample from the subject; and
- b) detecting the presence of a (GGC)<sub>12</sub> trinucleotide repeat at positions corresponding to positions -928 to -963 in the 5' end of the subject's bone morphogenetic protein receptor-II gene,

wherein the presence of the trinucleotide repeat indicates that the subject is either predisposed to, or afflicted with, Familial Primary Pulmonary Hypertension.

57-63. (canceled)

64. (amended) ~~The method of claim 2,~~ A method of detecting whether a subject is predisposed to, or afflicted with, a pulmonary hypertension which comprises (A) obtaining a suitable sample comprising a nucleic acid encoding bone morphogenetic protein receptor II from the subject; and (B) detecting in the nucleic acid encoding bone morphogenetic protein receptor II whether a mutation is present which is not present in a nucleic acid encoding wildtype bone morphogenetic protein receptor-II,

wherein the mutation described relative to a difference from the sequence encoding wildtype bone morphogenetic protein receptor II set forth in SEQ ID NO:1 is selected from the group consisting of:

- (1) a deletion of nucleotides having the sequence guanosine-guanosine-guanosine-guanosine-adenosine located at positions 1099-1103;
- (2) a deletion of a thymidine nucleotide located at position 2579;
- (3) a substitution of nucleotides having the sequence cytosine-thymidine-thymidine-thymidine located at positions 507-510 with nucleotides having the sequence adenosine-adenosine-adenosine;
- (4) a substitution of a cytosine nucleotide located at position 2617 with a thymidine nucleotide;
- (5) a substitution of nucleotides having the sequence adenosine-guanosine located at positions 690-691 with a thymidine nucleotide;

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(6) a substitution of a cytosine nucleotide located at position 1471 with a thymidine nucleotide;

(7) a substitution of a guanosine nucleotide located at position 1472 with an adenosine nucleotide;

(8) a deletion of nucleotides having the sequence adenosine-thymidine-thymidine-thymidine located at positions 1248-1251;

(9) a substitution of a cytosine nucleotide located at position 994 with a thymidine;

(10) a substitution of a thymidine nucleotide located at position 295 with a cytosine nucleotide;

(11) a deletion of a guanosine nucleotide located at position 1097;

(12) a substitution of a guanosine nucleotide located at position 727 with a thymidine nucleotide;

(13) a deletion of an adenosine nucleotide located at position 1214;

(14) a deletion of nucleotides having the sequence adenosine-cytosine located at positions 2441-2442;

(15) a substitution of a cytosine nucleotide located at position 2695 with a thymidine nucleotide;

(16) a deletion of 21 nucleotides located at positions 189-209;

(17) a substitution of a guanosine nucleotide located at position 296 with an adenosine nucleotide;

(18) a substitution of a thymidine nucleotide located at position 250 with a cytosine nucleotide;

(19) a substitution of a guanosine nucleotide located at position 1040 with an adenosine nucleotide;

wherein the presence of such a mutation indicates that the subject is predisposed, to or afflicted with, the pulmonary hypertension.

65. (amended) ~~The method of claim 3,~~ A method of detecting whether a subject is predisposed to, or afflicted with, a pulmonary hypertension which comprises (A) obtaining a suitable sample comprising bone morphogenetic protein receptor II from the subject; and (B) detecting in the bone morphogenetic protein receptor II whether a mutation is present which is not present in wildtype bone morphogenetic protein receptor-II,

wherein the mutation described relative to a difference from the wildtype bone morphogenetic protein receptor II sequence set forth in SEQ ID NO:2 is selected from the group consisting of:

(1) a mutation at a glutamic acid residue located at position 368 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(2) a mutation at an asparagine residue located at position 861 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(3) a substitution of a cysteine residue located at position 169 which causes premature termination of the protein sequence;

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(4) a substitution of an arginine residue located at position 873 which causes premature termination of the protein sequence;

(5) a mutation at a lysine residue located at position 230 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(6) a substitution of an arginine residue located at position 491 with a tryptophan residue;

(7) a substitution of an arginine residue located at position 491 with a glutamine residue;

(8) a substitution of a phenylalanine residue located at position 417 which causes premature termination of the protein sequence;

(9) a substitution of an arginine residue located at position 332 which causes premature termination of the protein sequence;

(10) a substitution of a cysteine residue located at position 99 with an arginine residue;

(11) a mutation at a proline residue located at position 366 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(12) a substitution of a glutamic acid residue located at position 243 which causes premature termination of the protein sequence;

(13) a mutation at an aspartic acid residue located at position 405 which causes the protein sequence thereon to

be different from the wildtype bone morphogenetic protein receptor II sequence;

(14) a mutation at a histidine residue located at position 814 which causes the protein sequence thereon to be different from the wildtype bone morphogenetic protein receptor II sequence;

(15) a substitution of an arginine residue located at position 899 which causes premature termination of the protein sequence;

(16) a deletion of consecutive amino acids having the sequence serine-threonine-cysteine-tyrosine-glycine-leucine-tryptophan located at positions 64-70;

(17) a substitution of a cysteine residue located at position 99 with a tyrosine residue;

(18) a substitution of a cysteine residue located at position 84 with an arginine residue;

(19) a substitution of a cysteine residue located at position 347 with a tyrosine residue;

wherein the presence of such a mutation indicates that the subject is predisposed, to or afflicted with, the pulmonary hypertension.